The National Committee for Mental Hygiene has created a subcommittee on furnishing hospital units for nervous and mental disorders to the United States Government, the project having been approved by Surgeon General W. C. Gorgas of the U. S. Army.

This subcommittee, of which Dr. Pearce Bailey of New York is chairman, is authorized to secure the services of alienists and neurologists to be commissioned in the Officers' Reserve Corps, Medical Section, and to serve in the neuro-psychiatric units which are to be attached to the base and other hospitals of the military services of the United States. Further information will be given, and application forms sent to physicians qualified in this branch of medicine, on application to The National Committee for Mental Hygiene, 50 Union Square, New York City.

The next evil which should be attacked with the utmost vigor by all boards of health is alcoholism. Public opinion needs to be enlightened on two points with regard to the use of alcohol as a beverage.

In the first place, it should be brought home to the entire population that the habitual use of alcoholic beverages reduces, in a serious degree, the productive efficiency of the community.

In the second place, recent experiments on the effects of alcohol on the nerves and glands of the human body have demonstrated beyond a doubt that alcohol invariably does harm, and never any good either in health or disease. The use of alcohol as a defense against exposure or fatigue has been given up by all sensible persons.

The evil is rooted, first, in what are called vested interests—that is, in the investment of large amounts of capital in the plants which produce, store and distribute beers, wines and spirits; and secondly, in the methods of taxation to which the white nations are accustomed. Heretofore the medical profession and the public health officers have given an uncertain sound concerning the use of alcohol.

It remains for the boards of health to attack this hideous evil with the weapons and in the spirit of preventive medicine. They should bring to the work all recent knowledge concerning the effects of alcohol on the human body, call to their aid legislators who can find equivalents for the public revenue now derived from the manufacture and sale of alcoholic drinks, and re-enforce to the utmost the wise counsellors who by moral teachings have brought about during the past fifty years considerable improvements in regard to the use of alcohol in the more intelligent and conscientious classes.—Haven Emerson, M. D., Amer. Jour. Pub. Health, June, 1917.

Original Articles

SOME HEART PROBLEMS SUGGESTING THE NECESSITY FOR A CLOSER ALLIANCE BETWEEN THE PHYSIOLOGISTS, BIO-CHEMISTS AND CLINICIAN.*

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For at least five years physiologists have agreed that lack of oxygen in the *blood* is rarely a stimulant to the respiratory center, but that the very slightest increase of carbon dioxide, resulting from any increase in the body processes, at once augments the rate and depth of respiration to such an extent that the additional inspired air furnishes enough oxygen to supply the new demand. Nevertheless, the great majority of clinicians still explain the symptoms of cardiac dyspnœa, and base their treatment on the older supposition.

In the *Journal of the American Medical Association* (November 4, 1911), the writer published a paper in which attention was called to the observations of Martin Flack, as well as those of Bachman, regarding the toxic effect of lactic acid upon the heart; likewise to the researches of Ryffel and others into the sources and fate of lactic acid in the human body, and expressed the hope that the laboratory work of these different investigators would lead to a more rational and successful cardio-therapy than that at present in vogue.

As full references to the work done by these gentlemen will be found in the article above mentioned it is unnecessary to repeat them in detail. Nine years ago Flack showed that if a frog's ventricle is placed in a weak solution of lactic acid (1 in 10,000 normal saline solution) the contractions become less and less, so that finally the ventricle stops in a state of complete relaxation; and about the same time Bachman, by perfusing rabbits' hearts with solutions of lactic acid obtained increased rate with greatly diminished force of contraction and a simultaneous dilatation of the coronary arteries, a fact that would indicate lactic acid to be a paralyzing agent for all muscles of the cardio-vascular system; neither did it require a strong solution, but even amounts so small as those occasionally found in the blood of a normal rabbit had some paralyzing effect.

One of the first thoughts suggested by these experiments is an interpretation of what we call acute dilatation of the heart as it occurs during exertion, a condition that is generally described as if it were a purely mechanical effect of "heart strain." Most of us are familiar with the breakdowns that take place during or immediately after an athletic contest, and have seen them in varying degrees of severity, some when the heart recovered its normal dimensions within two or three days, and others where the change was more prolonged or even permanent. Ryffel (*Quarterly Journal of Medicine*, Vol. 3, No. 10, January, 1910), found the lactic acid in urine from competitors in a

* Read before the St. Francis Hospital Clinical Society, March 31, 1916.

twenty-four hours' track walking race in no case above 6.5 mg. per hour, but obtained relatively large quantities from that passed following violent exercise, 430 mg., subsequent to 0.36 mile, and 818 mg. after 0.6 mile, running as fast as possible round a track thirty-three laps to the mile. The lactic acid in the blood, taken from a vein in the forearm immediately after the exercise, was also increased in one case from 12.5 mg. at rest to 70.8 mg. per 100 c.c. Excess of lactic acid disappeared from the urine in about thirty minutes after stopping, but in forty-five minutes the lactic acid of the blood was not quite reduced to normal. The older observers supposed that the production of lactic acid by muscle depended on its long-continued activity, but evidently this is not the case, and the important factor is the relation between the activity of the muscles and their supply of oxygen. The increased respiration of exercise has more effect in removing carbon dioxide than lactic acid, so that in course of time the carbon dioxide pressure becomes low, whilst the acidity of the blood is still high, and the latter is only gradually diminished after the cessation of the exercise by oxidation of the lactic acid and excretion of urine containing an excess of lactic acid, this process occupying about one hour after short periods of violent activity.

Here is some laboratory work that is absolutely pregnant with matters of importance to the clinician, and yet they are practically ignored by the vast majority. Take for example its relation to the hearts of athletes. It is exceptional in the universities and public schools that the hearts of members of the various athletic teams are examined after exercise; most of them are examined before admission to the team, and if the heart appears to be normal they are told to go ahead, and no further notice is taken of them unless they complain or show marked signs of distress. Each year, generally when the excitement of the season is over, for we all know how a boy hates to be a "quitter," a number apply for treatment on account of palpitation or some other cardiac discomfort, and it takes months to get their hearts reduced to the normal area, indeed some of them never do fully recover. It is highly improbable that these changes in the myocardium are due to a *simple* strain, such as might result from lifting a heavy weight, but rather they are the outcome of repeated intoxications of the cardiac muscle with lactic acid. It is not permissible to say that because acid is quickly eliminated during the period of rest that it therefore cannot do much harm; the effects persist after the elimination of the toxin; a fire travels quickly through a forest, but it takes a long time for the trees to grow again.

These observations on the production of lactic acid and its influence on the cardio-vascular system furnish us with a definite physiological basis on which we can frame an opinion regarding the nature and amount of exercise that may be allowed to different individuals. The term "heart strain" is so very vague that there is much difficulty in estimating what it constitutes, but since we know that exertion generates a toxin which is injurious to the myocardium, and as it has been demonstrated that the amount of toxin produced varies with the demand for *rapid* oxidation rather than with the duration of the effort we are in a much better position than formerly to decide what exercises are most trying to the heart. But the distinctive idiosyncrasy of each case must always be taken into account, for we all know that the susceptibility of normal hearts to toxins varies in different individuals, the influence of tobacco being a familiar example, and consequently much of this trouble could be avoided by examining the heart immediately after exercise. Because a boy cannot stand one form of athletic exercise it does not follow that he must be excluded from all others. Personal experience with participators in college sports has led me to the conclusion that track and oarsmen suffer most, then football and tennis players, and lastly, the baseball men; of course, it must be understood that these remarks apply to men who are exerting themselves under the stimulus of competition. At one time I thought it was otherwise, and used to forbid football where I allowed the more refined and gentle sport of track work, but experience made me change my opinion, and come to the conclusion that while the footballer took bigger chances on his bones and his neck, he was not so liable to injure his heart as was the sprinter and hurdler.

These observations on lactic acid also suggested the idea that much of the suffering experienced in senile hearts, associated with varying degrees of arterio-sclerosis, might result from the presence of lactic acid in the blood. The type of case is familiar to every physician. The patient is generally over fifty-five years of age, and in the early stage does not show any signs of dropsy or oedema, but his chief complaint is rather of weakness, or easily induced fatigue; he feels slightly dyspnœic on trivial exertions, such as bending over to lace his shoes in the morning, or performing his toilet, and the trouble may increase until not only is he always conscious that his breathing is abnormal, but paroxysms of increased severity are readily induced by excitement, exertion, or a variety of other causes. Or there may be gastric distress, such as a craving sensation in the stomach, but an absolute disgust for food the moment it is placed before him. The expression is keen and alert, altogether different from the dull condition so common in cases of valvular disease where there is pulmonary congestion with oedema, bronchitis and possibly pleural effusion as a result of failed compensation. Of course the two types may co-exist, but I believe an associated arterio-sclerosis is essential to the production of the first group of symptoms.

It may be of interest to the physiologist and biochemist to follow the vagaries of a clinician's mind in his endeavor to utilize their observations in the treatment of his patients.

The plan of campaign adopted, just prior to the writing of my paper in 1911, was two-fold: (1) To neutralize existing acids in the blood; (2) to find the source and fate of lactic acid in the body,

and try to influence those in the patient so that the balance between its formation and elimination might be restored.

It is now nearly five years since this treatment was begun, but I cannot remember any case where the patient's condition seemed to be improved by the use of alkalies; indeed the only two drugs that seemed to be of any permanent value were the iodide of potash and the protoiodide of mercury, both of which belong to the alterative group. The failure of soda to furnish relief was particularly disappointing because the good results so frequently attributed to its administration in the acidosis of diabetes has encouraged the expectation that not only would it aid in transporting carbon dioxide from the tissues to the lungs, but that, by increasing the alkalinity of the blood it would remove the irritation from the respiratory centre.

In his third Herter lecture, delivered at Johns Hopkins Hospital, October, 1914 ("Lectures on the Heart," by Thomas Lewis, published by Paul B. Hueber, New York), Dr. Thomas Lewis expresses the opinion that much of the cardiac dyspnœa is due to a diminished alkalinity of the blood from the presence of lactic and other acids at present unknown. He does not make any suggestions in regard to treatment, but further states that a characteristic of the alveolar air in these cases is "high oxygen and low carbon dioxide content"; that "the blood is fully aerated and has a low tension of carbon dioxide."

My conclusions from such findings would be that the symptoms cannot be attributed to lack of oxygen or excess of carbonic acid in the blood, but that there appears to be deficient oxidation in the tissues, either because the oxygen in the blood cannot reach them, or because, on account of the absence of some enzyme or other necessary agent, the tissues cannot utilize the oxygen supplied to them.

The presence of lactic acid in the blood is an evidence of deficient oxidation. The sources of lactic acid in the human body are the metabolism of glucose in muscles during their activity, and to a lesser extent from the proteid substance, and it also arises from glucose and other carbo-hydrates during constructive metabolism. That the destruction of lactic acid in the muscles and in the body generally depends upon an adequate supply of oxygen has been shown by several observers, and, as Stoklasa discovered a ferment both in muscle and blood that converted lactic acid into alcohol and carbon dioxide, it is possible that the oxidation takes place through some such indirect process. In the normal person an excess of lactic acid arising from severe exertion or other causes, stimulates the respiratory center until the greater ventilation of the lungs provides enough oxygen to compensate for this increase, and the subject therefore quickly recovers even from severe dyspnœa when he comes to rest. Furthermore, although the previous inhalation of oxygen enables an athlete to undertake exertion with much less discomfort, to the cardiac dyspnœic of the type under consideration the administration of oxygen brings no relief, and consequently we are forced to the belief that in his case some connecting link between the supply and utilization of oxygen has been lost. If it be true, as held by many physiologists, that the interchange of gases between the blood and tissues is not simply a matter of diffusion, but that the capillary walls have secretory power that causes them to play an active part in this process, we can see how in advanced cases of arterio-sclerosis, with many capillaries destroyed and others impaired, oxidation in the tissues may be imperfect so that lactic acid is not destroyed, but enters the blood and by reducing its alkalinity diminishes its capacity for transporting carbon dioxide which will accumulate in the tissues and cause a gradually increasing tissue asphyxiation. Or more probably the defective circulation consequent upon arterial changes impairs the nutrition of the glands and other tissues in which enzymes are formed, so that there is a scarcity of these necessary to complete the oxidation of lactic or any other acids which may be formed in the processes of constructive and destructive metabolism. This would probably explain the benefit that follows the prolonged use of alteratives such as the iodides of potash or mercury, which are known to have a very powerful influence on the glandular structures and nutritive processes of the body, although the manner in which they attain this end is still a matter of conjecture. The failure of the different alkalies when given by the mouth to influence the dyspnœa was a great disappointment because a diminished alkalinity has been shown to exist in this type of dyspnœa and there can be no doubt that the presence of acid in the blood, even in minute quantities, stimulates the respiratory center to greater activity. Bicarbonate of soda was given because of its great reputation as an atacid, especially in acidosis, potassium citrate because of its vaunted ability to render the urine and blood alkaline, as well as on account of the claim that in cases of lithæmia it promotes oxidation; citrate of soda for the reason that it is supposed to enter the blood as such where it is converted into carbon dioxide and sodium carbonate, thereby increasing the alkalinity of the blood and urine, and being eliminated in the urine as a carbonate. Sodium phosphate was the last selection made, and this was tried for the reason that physiologists have found that it re-acts towards carbon dioxide much in the same way as blood; so that formerly it was thought that phosphates in the blood plasma were an important factor in the evolution of the carbon dioxide. The chloride and lactate of calcium were also used, but failed to relieve the dyspnœa, in fact none of the preparations mentioned yielded the desired results. In stating that these different salts are supposed to have an alkalizing effect on the blood I am not giving my own opinion, but simply repeating the statement made by many writers; the data upon which their conclusions are based are not mentioned, but it would appear to be the opinion that because the alkalinity of the urine is increased, a similar change must take place in the blood. It is extremely doubtful whether alkalies or acids *taken into the stomach* ever materially affect the blood reaction. This opinion is based not only on such therapeutic

failures as those just mentioned, but also upon the general experience that such preparations as citric or lactic acid may be given in sufficient quantities to produce an extreme and even painful acidity of the urine without inducing any of the cardiac symptoms described by physiologists as accompanying the injection of even a minute quantity of acid in the blood. There is some provision of nature to maintain the blood reaction fairly constant during health, else there would be a continual variation with every meal according to the amounts of acids and alkalies ingested, and this protective influence cannot always be ascribed to a neutralizing combination with other food stuffs, as the result is the same when they are taken alone. It would look as though they entered into some combination in the lymph or tissues before entering the blood that rendered them ineffective, and that their elimination in the urine was accomplished by the decomposition of these compounds through the secretory activity of the kidney. The general acceptation appears to be that all alkalies are neutralized by the carbonic acid of the tissues and circulate in the blood as neutral bicarbonates without altering its reaction; and that while an excessive supply of alkali, by combining with the body acids, might be expected to render the tissues more alkaline, this is obviated by the rapidity with which the excretory glands remove the excess.

In this way there is more *available alkali* in the blood and tissues during alkali treatment, but it can be utilized in the neutralization of acids only when the carbon dioxide can be removed from the neutral salts. The clinician must therefore inquire from the bio-chemist and physiologist whether in some of our cases of arterio-sclerosis there may not be changes in the tissue cells that retard such chemical processes or make them impossible.

This question is permissible because observations both upon men and animals warrant the conclusion that the alkaline carbonates which are prescribed or taken in various waters for their antacid effect, when administered by the stomach do not exhibit the toxic effects of the sodium and potassium ions upon the cardiac muscle and other tissues because they are so rapidly excreted by the kidneys. Probably this is perfectly true in the healthy man, but is it equally so in disease? Vichy water abounds in alkaline bicarbonates and is used with impunity by the majority of people, yet there are others to whom the treatment at the spa is refused, and I am informed that this rule includes all cases of cardiac asthenia. Personally I have had a number of patients who, while using Vichy water on account of its excellent antacid effects, became depressed, languid, averse to muscular exertion, and dyspnœic. Improvement followed rapidly upon discontinuance of the water, and upon its resumption the symptoms soon returned. I have seen symptoms of cardiac dyspnœa with reduced blood pressure occur in patients who were taking from twenty to thirty grains of potassium iodide daily, while a change to one of the preparations of calcium iodide or hydriodic acid obviated any unpleasant symptoms. This is the exception rather than the rule in patients suffering from arterio-sclerosis and there do not appear to be any special physical signs in the heart or blood vessels that aid in identification of the susceptible group. Hence the question has to be asked whether the interchanges that normally take place between chemical substances within the body are not facilitated by some functional activity of the tissue cells, and whether apparent discrepancies between the conclusions arrived at from experiment or observations of healthy subjects and the results obtained by the clinician at the bedside are not due to changes in the tissue cells. In regard to treatment this is of importance because an affirmative answer would imply that the practitioner must not content himself with any halfway measures, as for example an attempt to neutralize excessive acidity, but must also endeavor to restore the function to the diseased tissue cell or in some way compensate for it. We have an example of the latter in the treatment of myxœdema by the administration of thryroid gland preparations.

Outside the body oxidation is accelerated by the presence of an alkali, and consequently, alkalies have been administered in the hope of producing a more perfect metabolism; but, possibly on account of the rapidity with which the excess of alkali is eliminated or transformed into the neutral bicarbonate, the laboratory experiment does not find its homologue within the human body, at least the reported observations upon this subject are very contradictory. We expect that the true treatment of such cases must await the telling of the secrets of metabolism and organo-therapy, for the human body is neither a retort nor a test tube, but a whole chemical factory. At present I am treating some cases with thyroid extract, as that gland is reputed to play an important role in metabolism by promoting the oxidation of proteids, but the results are too imperfect for publication at the present time.

There is another feature regarding the dyspnœa of arterio-sclerotic patients that is worthy of consideration. Nervous irritability is one of the characteristic symptoms of arterio-sclerosis. These sufferers undergo a change of disposition, little things annoy them, and the consciousness of the fact annoys them still more, their emotions are more easily influenced than formerly, and either joy, sorrow or mental effort may induce an attack of dyspnœa. It seems to me that in many instances the respiratory center participates in this cerebral hyperaesthesia, so that normal quantities of carbon dioxide or any of the acid products of metabolism may more readily induce increased respiratory movements, in other words, that in some cases the cardiac dyspnœa may be due more to hyperaesthesia of the respiratory center than to diminished alkalinity of the blood. Recognition of this condition explains the dyspnœa that awakens the patient from his sleep, because it is generally admitted that this hyperaesthesia is the result of impaired cerebral nutrition; and during sleep the fall of cerebral blood pressure and the shrinking of

the brain substance in consequence of vascular relaxation throughout the body generally still further impairs the nutrition and increases the irritability of the respiratory center so that it responds to a stimulus from blood in which, as metabolism is diminished at this time, there is no reason to expect excess either of carbon dioxide or any other form of acidity. Sometimes the condition is relieved by a combination of digitalis or strophanthus or caffeine with one of the nitrites, as it would seem that a combination of a vaso-dilator and cardiac stimulant is more effective in maintaining an adequate circulation through the sclerosed vessel, thereby removing the irritability of the nerve centers arising from impaired nutrition, but in a very large number of cases the patient's distress is not relieved until small doses of morphine, one thirty-second or one twenty-fourth of a grain, every eight hours, are added to the mixture.

The most complete discussion of this subject with which I am familiar can be found in a composite article by Lewis, Ryffel, Wolf, Cotton and Barcroft, entitled "Cardiac and Renal Dyspnœa," that was published in *Heart,* Vol. 5, No. 1, 1913. This investigation consisted in a most elaborate examination, at the bedside and in the laboratory, of fifteen patients; and although ten of that number had pleural effusion, ascites or general dropsy, still, in the judgment of these gentlemen, such mechanical obstructions to respiration were not sufficient to explain the degree of dyspnœa. This is perfectly possible but, as it is a question of individual judgment, those readers who have not seen the patients cannot help wishing that such respiratory embarrassments had not existed. It is interesting to note that abnormal fullness of the veins is mentioned as one of the clinical features in thirteen out of the fifteen cases, no reference being made to the condition of the veins in the other two patients; and in only two of the whole series of fifteen cases was cyanosis well-marked, in the others it was very slight or entirely absent. In only one case did the haemoglobin fall below 75 per cent., and in the others it ranged from 80 to 102 per cent. In all of the patients there was some degree of acidosis or diminished alkalinity of the blood. They express the opinion "that as no evidence of the formation of an abnormal amount of any organic acid is to be obtained from examination of the urine, so this acidosis appears to be another instance of the same phenomena of the retention of acids in excess of bases which is shown during residence at high altitudes." The thought, therefore, was perfectly natural that if these forms of cardiac dyspnœa resemble that of high altitudes some benefit might be expected from a line of treatment calculated to produce changes in the blood similar to those that occur during the process of adaptation. This consists in an increase of red corpuscles to seven or eight millions per c. m. m., at first probably by concentration of the blood, but ultimately from increased activity of the blood-forming organs. During the establishment of adaptation the pulse rate is accelerated so that in the rarefied atmosphere adequate oxygenation will take place by blood abnormally rich in haemoglobin circulating more rapidly. Most of my cases have shown haemoglobin to be present only in the proportion of from 65 to 85 per cent., and under the administration of arsenic and iron there was some improvement, but not enough to awake enthusiasm. A review of the tabulated statement of the gentlemen already mentioned is no more encouraging, as they report cases of orthopnœa in which there were five and even six million red corpuscles to the c. m. m., with from 95 to 102 per cent. haemoglobin.

The failure of alkaline treatment and inhalations of oxygen to relieve the dyspnœa, together with the co-existence of full veins, abundance of red corpuscles with high color index, and the absence of cyanosis still farther impresses one with the ideas already mentioned that in arterio-sclerosis there is some flaw which prevents the tissues from utilizing the oxygen supplied to them, and suggests diminished function owing to degenerative changes in the vascular endothelium as a possible cause. For many years evidence has been accumulating that these cells have distinct chemical functions, and the recent work of Hooper and Whipple, who have shown by experiments upon animals whose livers had been excluded from playing any part in the process, that vascular endothelium in common with the mesothelium of the pleura and peritoneum have the power of transforming haemoglobin into bilirubin by splitting off the iron from the former demonstrates conclusively that these cells can no longer be regarded only as having a mechanical function, such as affording protection to different surfaces or forming a system of tubes for conveying the blood throughout the body, but that they are active participators in the chemical processes of the body. Possibly the foregoing remarks may cause some amusement to the physiologist or bio-chemist, because the problems are so self-evident to him, but on the other hand, the clinician not infrequently smiles at the dogmatism of laboratories and admires the unblushing assurance with which at some subsequent period, a stoutly defended theory is discarded as absolutely untenable.

Nevertheless, on this occasion I am willing to be the scapegoat if the sacrifice makes plain the necessity for a closer association between the different departments of medicine, and emphasizes to our undergraduates that anatomy, physiology and chemistry are not studies preliminary to medicine which may be neglected so soon as a diploma is obtained, but that they, too, are progressive subjects, that the anatomist, physiologist and chemist have still much to learn, and that as the clinician is the man who must utilize and turn to practical account the discoveries of these other gentlemen he can only hope to do so if he keeps himself informed regarding the work that they are doing.

The scope of medicine is too great for a man to do this by his own effort; it is only possible for him to attain this end when he is so situated as to confer at will with the individual observers or to hear from them at intervals a summary of the progress made in their departments.